

In the Specification

Applicant presents replacement paragraphs below indicating the changes with insertions and deletions indicated by underlining and strikeouts, respectively.

Please delete the paragraph beginning at page 24, line 7 and replace it with the following:

The permutation distribution was used to assess the significance of t-statistics calculated for each gene in the dataset (Permax test). The customized program written in S-plus language to calculate Permax is a data analysis software tool for testing the significance of gene expression. It has been presented by Mutter, et al., 8th International Workshop on Chromosomes in Solid Tumors, Tucson, AZ, 2000; and is available online from the website of the Dana Farber Cancer Institute, laboratory of Dr George Mutter ² ~~at~~ ~~biowww.dfei.harvard.edu/~gray/permax.html~~] and from Robert J. Gray, Department of Biostatistical Science, Dana-Farber Cancer Institute, 44 Binney Street Boston, MA 02115. Permax details enclosed therein are incorporated by reference herein.. In this approach all 1001 possible ways of dividing the 14 samples into two groups of sizes 4 and 10 were considered. For each of these, the t-statistics were computed for each gene. With unequal group sizes, these distributions are not symmetric, so the significance was assessed separately in each direction. To control the overall error rate, the distributions of the maximum and minimum t-statistics over the genes were used. That is, for each gene, the p-value in the direction with expression higher (lower) in normals is the proportion of permutations with the minimum (maximum) t statistic over all genes less than (greater than) or equal to the observed value for the particular gene. A test declaring as significant any genes with say $p < .50$ then guarantees that the chance of any false positives being selected is $< 50\%$.

Please delete the paragraph beginning at page 29, line 7 and replace it with the following:

2. Gray, R. Permax available online from the Dana Farber Cancer Institute in the laboratory of Dr George Mutter. On Line. Available:
~~http://biowww.dfei.harvard.edu/~gray/permax.html~~ 2000.

3. National Center for Biotechnology Information (USA): Unigene available on line
C² from the National Center for Biotechnology Information. Online. Available: <http://www.ncbi.nlm.nih.gov/UniGene/> 2000.

5. National Center for Biotechnology Information (USA): Locuslink available on line
N/E from the National Center for Biotechnology Information Online. Available: <http://www.ncbi.nlm.nih.gov/LocusLink/> 2000.